REMARKS/ARGUMENTS

Claims 1, 3-7, 12-15 and 17 are pending. By this Amendment, claims 2, 8-11 and 16 are cancelled and claims 1, 3-7, 12 and 14 are amended. Support for the amendments to claims 1, 3-7, 12 and 14 can be found, for example, in original claims 1-17. No new matter is added. In view of the foregoing amendments and following remarks, reconsideration and allowance are respectfully requested.

Rejection Under 35 U.S.C. §102

The Office Action rejects claim 16 under 35 U.S.C. §102(b) over WO 01/56983 to Cazer et al. ("Cazer"). By this Amendment, claim 16 is cancelled, rendering the rejection moot. Accordingly, withdrawal of the rejection is respectfully requested.

Rejection Under 35 U.S.C. §103

A. Cazer

The Office Action rejects claims 1-15 and 17 under 35 U.S.C. §103(a) over Cazer. By this Amendment, claims 2 and 8-11 are cancelled, rendering the rejection moot as to those claims. As to the remaining claims, Applicants respectfully traverse the rejection.

Claim 1 recites "[a] crystalline, hydrated form of a sodium salt of 3-pyridyl-1-hydroxyethylidene-1,1-bisphosphonic acid, wherein: the form is a pentahydrate of a monosodium salt of 3-pyridyl-1-hydroxyethylidene-1,1-bisphosphonic acid; the form contains from 20 to 23 weight % of water built in the crystal lattice based on a total weight of the molecule; and the form contains from 5.5 to 7.5 weight % of sodium based on the total weight of the molecule" (emphasis added). Cazer does not disclose or suggest such a form.

The Office Action asserts that Cazer discloses monohydrate and hemipentahydrate forms of sodium salts of risedronic acid. *See* Office Action, page 2. The Office Action

concedes that Cazer fails to disclose the percentages of sodium recited in the present claims, but asserts that it would have been obvious to modify the compositions of Cazer to obtain such percentages. *See* Office Action, page 3. As noted above, claim 1 of the present application is directed to a pentahydrate of a monosodium salt of risedronic acid. Cazer discloses only monohydrates and hemipentahydrates of salts of risedronic acid. As Cazer fails to disclose or suggest a pentahydrate of a monosodium salt of risedronic acid, Cazer fails to disclose or suggest each and every feature of claim 1.

Moreover, the present specification demonstrates the superiority of the pentahydrate of a monosodium salt of risedronic acid of claim 1 relative to the hemipentahydrates of Cazer. For example, in the present specification, the solubility of the pentahydrate of claim 1 in simulated gastric fluid (0.1 M HCl) was compared to the solubility of a hemipentahydrate according to Cazer in such simulated gastric fluid. *See* present specification, page 9, lines 3 to 18. Under like conditions, the hemipentahydrate of Cazer dissolved sufficiently to provide a concentration of 874 mg/l of hemipentahydrate in the simulated gastric fluid, while the pentahydrate of claim 1 dissolved sufficiently to provide a concentration of 2,418 mg/l of pentahydrate. *See* present specification, page 9, lines 7 to 9, 13 to 15. Such better solubility of the pentahydrate of claim 1 in gastric fluid suggests that an oral composition including the pentahydrate would provide superior bioavailabilty relative to the hemipentahydrate of Cazer.

In addition, the present specification demonstrates the polymorphic stability of pentahydrate of claim 1. Cazer indicates that the hemipentahydrate is thermodynamically preferred form of the various hydration states of the monosodium salt of risedronic acid, noting that the monohydrate typically will convert to the hemipentahydrate under typical processing conditions. *See* Cazer, page 2, lines 23 to 28. Contrary to this assertion, the present specification demonstrates that the pentahydrate of claim 1 is at least as stable as the hemipentahydrate of Cazer. *See* present specification, page 7, lines 3 to 6. In particular,

when the pentahydrate of claim 1 is dried to have a water content slightly less than the water content of the hemipentahydrate of Cazer (*see* Cazer, page 3, line 7) and subsequently allowed to rehydrate, the pentahydrate does not convert to the hemipentahydrate, but rather returns to the stable pentahydrate state. *See* present specification, page 7, lines 3 to 6. Accordingly, the present specification demonstrates that the present inventors discovered a novel form of monosodium salt of risedronic acid that is stable and provides superior solubility in gastric fluid relative to the compositions disclosed in Cazer.

As explained, claim 1 would not have been rendered obvious by Cazer. Claims 3-7, 12-15 and 17 depend from claim 1 and, thus, also would not have been rendered obvious by Cazer. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

B. Aronhime

The Office Action rejects claims 1-17 under 35 U.S.C. §103(a) over WO 03/086355 to Aronhime et al. ("Aronhime"). By this Amendment, claims 2, 8-11 and 16 are cancelled, rendering the rejection moot as to those claims. As to the remaining claims, Applicants respectfully traverse the rejection.

Claim 1 is set forth above. The Office Action asserts that Aronhime discloses polymorphs and pseudo-polymorphs of risedronate sodium. *See* Office Action, page 3. The Office Action concedes that Aronhime fails to disclose the particular water and sodium contents recited in claim 1, but asserts that it would have been obvious to modify the compositions of Aronhime to obtain such water and sodium contents. *See* Office Action, page 3. Notwithstanding these assertions, the Office Action fails to demonstrate how Aronhime discloses or suggests the particular form of a sodium salt risedronic acid recited in claim 1.

As indicated above, claim 1 requires a pentahydrate of a monosodium salt of risedronic acid. Characteristics of the pentahydrate include 20 to 23 weight % of water built in the crystal lattice based on a total weight of the molecule and 5.5 to 7.5 weight % of sodium based on the total weight of the molecule. Aronhime includes no indication that any of the various disclosed risedronate sodium compositions are pentahydrates. Moreover, none of the risedronate sodium compositions of Aronhime are indicated to have the water and sodium contents recited in claim 1.

The Office Action asserts that one of ordinary skill in the art would have been motivated to modify the risedronate sodium compositions of Aronhime to obtain a pentahydrate having the water and sodium contents recited in claim 1, but provides no indication of why one of ordinary skill in the art would have been motivated to do so. The present inventors discovered a novel form of monosodium salt of risedronic acid that is stable and provides superior solubility in gastric fluid, as discussed above. It is only with the guidance of the present specification that one of ordinary skill in the art would have been led to prepare the particular form of claim 1. As is well settled, motivation to modify the teachings of a prior art reference must come from the prior art, and not from Applicants' own disclosure.

As explained, claim 1 would not have been rendered obvious by Aronhime. Claims 3-7, 12-15 and 17 depend from claim 1 and, thus, also would not have been rendered obvious by Aronhime. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Conclusion

For the foregoing reasons, Applicant submits that claims 1, 3-7, 12-15 and 17 are in condition for allowance. Prompt reconsideration and allowance are respectfully requested.

Respectfully submitted,

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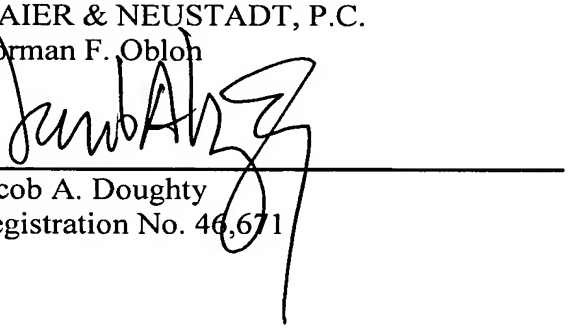

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